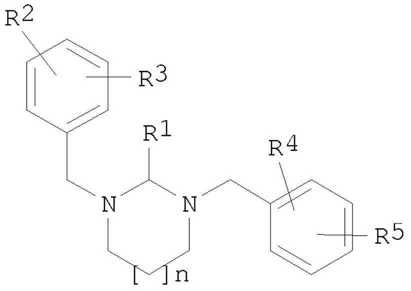
```
Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSPTAJDA1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  DEC 01  ChemPort single article sales feature unavailable
 NEWS  3  APR 03  CAS coverage of exemplified prophetic substances
                  enhanced
 NEWS  4  APR 07  STN is raising the limits on saved answers
 NEWS  5  APR 24  CA/CAplus now has more comprehensive patent assignee
                  information
 NEWS  6  APR 26  USPATFULL and USPAT2 enhanced with patent
                  assignment/reassignment information
 NEWS  7  APR 28  CAS patent authority coverage expanded
 NEWS  8  APR 28  ENCOMPLIT/ENCOMPLIT2 search fields enhanced
 NEWS  9  APR 28  Limits doubled for structure searching in CAS
                  REGISTRY
 NEWS 10  MAY 08  STN Express, Version 8.4, now available
 NEWS 11  MAY 11  STN on the Web enhanced
 NEWS 12  MAY 11  BEILSTEIN substance information now available on
                  STN Easy
 NEWS 13  MAY 14  DGENE, PCTGEN and USGENE enhanced with increased
                  limits for exact sequence match searches and
                  introduction of free HIT display format
 NEWS 14  MAY 15  INPADOCDB and INPAFAMDB enhanced with Chinese legal
                  status data
 NEWS 15  MAY 28  CAS databases on STN enhanced with NANO super role in
                  records back to 1992
 NEWS 16  JUN 01  CAS REGISTRY Source of Registration (SR) searching
                  enhanced on STN

 NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN customer
  agreement.  This agreement limits use to scientific research.  Use
  for software development or design, implementation of commercial
  gateways, or use of CAS and STN data in the building of commercial
  products is prohibited and may result in loss of user privileges
  and other penalties.

* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:39:41 ON 11 JUN 2009
```

```
=> file registry
COST IN U.S. DOLLARS                             SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    0.22       0.22

FILE 'REGISTRY' ENTERED AT 15:39:53 ON 11 JUN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    9 JUN 2009  HIGHEST RN 1154896-16-8
DICTIONARY FILE UPDATES:   9 JUN 2009  HIGHEST RN 1154896-16-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s cyclopamine/cn
L1           1 CYCLOPAMINE/CN

=> file hcaplus
COST IN U.S. DOLLARS                             SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    5.83       6.05

FILE 'HCAPLUS' ENTERED AT 15:40:11 ON 11 JUN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 11 Jun 2009  VOL 150 ISS 24
FILE LAST UPDATED: 10 Jun 2009  (20090610/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Feb 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.
```

```
CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l1
L2         198 L1

=> s l2 and psoriasis
         19153 PSORIASIS
L3           7 L2 AND PSORIASIS

=> d l3 1-7 ibib, abs

L3   ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2007:1392120  HCAPLUS
DOCUMENT NUMBER:         148:24502
TITLE:                   Hexahydropyrimidine derivatives, tetrahydroimidazole
                         derivatives, and octahydroazepan derivatives, and
                         their therapeutic use
INVENTOR(S):             Westman, Jacob; Toftgaard, Rune; Lauth, Mattias;
                         Teglund, Stephan
PATENT ASSIGNEE(S):      Actar AB, Swed.
SOURCE:                  PCT Int. Appl., 55pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
     WO 2007139492        A1    20071206    WO 2007-SE50352         20070524
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,
             GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
             KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK,
             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                      SE 2006-1188        A  20060530
OTHER SOURCE(S):         MARPAT 148:24502
GI
```



I

```
AB   The invention discloses compds. I [R1 = (un)substituted (un)branched
     (un)saturated C3-12 cycloalkyl and C1-10 alkyl, etc.; R2-R5 = H, halo, OH,
     etc.; n = 0-2] for use as medicaments.  The medicaments are suitable for
     the treatment of conditions such as cancer, keloids and granulomatous skin
     disorders, psoriasis, pathol. neovascularization, excessive hair
     growth and excessive body weight and for inhibition of stem cell
     proliferation and induction of differentiation after spinal cord injury
     and CNS diseases.  The invention also discloses a method for treating a
     mammal by administration of I.
REFERENCE COUNT:         11    THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3   ANSWER 2 OF 7  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2007:227086  HCAPLUS
DOCUMENT NUMBER:         146:280997
TITLE:                   Hedgehog pathway antagonists to treat disease
INVENTOR(S):             Beachy, Philip Arden; Liu, Jun
PATENT ASSIGNEE(S):      The Johns Hopkins University, USA
SOURCE:                  PCT Int. Appl., 46pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE          APPLICATION NO.        DATE
     ---------------     ----   --------      --------------------   --------
     WO 2007024971        A2    20070301      WO 2006-US32952        20060822
     WO 2007024971        A3    20080103
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
     AU 2006283040        A1    20070301      AU 2006-283040         20060822
     CA 2619889           A1    20070301      CA 2006-2619889        20060822
     EP 1919480           A2    20080514      EP 2006-802186         20060822
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
             BA, HR, MK, RS
     JP 2009506054        T     20090212      JP 2008-528124         20060822
```

```
PRIORITY APPLN. INFO.:                      US 2005-710117P     P  20050822
                                            WO 2006-US32952     W  20060822
AB   Compds., compns., kits and methods for modulating hedgehog pathway
     activity, and treating conditions such as tumors related to abnormal or
     aberrant hedgehog pathway activity, are disclosed wherein the hedgehog
     antagonist is itraconazole.

L3   ANSWER 3 OF 7  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2006:213263  HCAPLUS
DOCUMENT NUMBER:         144:292926
TITLE:                   Methods for preparation cyclopamine analogs and use
                         thereof in treating cancers
INVENTOR(S):             Janardanannair, Somarajannair; Adams, Julian; Ripka,
                         Amy S.; Hospital, Marta R.; Tremblay, Martin
PATENT ASSIGNEE(S):      Infinity Pharmaceuticals, Inc., USA
SOURCE:                  PCT Int. Appl., 102 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2006026430        A2    20060309    WO 2005-US30406        20050826
     WO 2006026430        A3    20060622
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     AU 2005280112        A1    20060309    AU 2005-280112         20050826
     CA 2579078           A1    20060309    CA 2005-2579078        20050826
     US 20060074030       A1    20060406    US 2005-213534         20050826
     US 7230004           B2    20070612
     EP 1817308           A2    20070815    EP 2005-791140         20050826
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
             BA, HR, MK, YU
     CN 101044139         A     20070926    CN 2005-80035365       20050826
     JP 2008511635        T     20080417    JP 2007-530162         20050826
     BR 2005014444        A     20080610    BR 2005-14444          20050826
     MX 2007002342        A     20080627    MX 2007-2342           20070226
     IN 2007KN00744       A     20070713    IN 2007-KN744          20070228
     NO 2007001264        A     20070515    NO 2007-1264           20070308
     KR 2007083602        A     20070824    KR 2007-706979         20070327
     US 20070191410       A1    20070816    US 2007-737035         20070418
     US 7407967           B2    20080805
     US 20080269272       A1    20081030    US 2008-171208         20080710
PRIORITY APPLN. INFO.:                      US 2004-605020P     P  20040827
                                            US 2004-617170P     P  20041008
                                            US 2004-625676P     P  20041105
                                            US 2005-683169P     P  20050519
                                            US 2005-213534      A1 20050826
                                            WO 2005-US30406     W  20050826
```

US 2007-737035 A1 20070418
OTHER SOURCE(S): CASREACT 144:292926; MARPAT 144:292926
GI

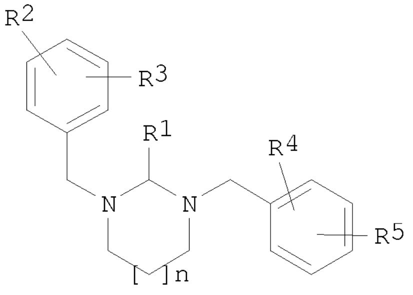
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides compns. and methods for modulating smoothened dependent pathway activation. The present invention provides analogs I [R1, R8 = H, alkyl, alkenyl, alkynyl, aryl cycloalkly, heterocyclylalkly, aralkyl, heteroaryl, heteroaralkyl, halo, SH, alkylthio, arylthio, aralkylthio, OH, alkoxy, aryloxy, acyloxy, NH2, mono- or dialkylamino, arylamino, acylamino, aralkylamino, NO2, acylthio, CONH2, SO2NH2, sulfate, etc.; R1 = sugar; R2, R9 = H, alkyl, alkenyl, alkynyl, aryl cycloalkyl, heterocyclylalkyl, CN, aralkyl, alkoxy, aryloxy, acyloxy, CO2H, halo, SH, alkylhio, arylthio, aralkylthio, OH, NH2, alkylamino, arylamino, acylamino, aralkylamino, etc.; R3, R4, R6, R7, R13, R14 = H, alkyl, alkenyl, alkynyl, aryl cycloalkyl, heterocyclylalkyl, aralkyl, alkoxy, aryloxy, acyloxy, halo, OH, NH2, alkylamino, arylamino, acylamino, aralkylamino, heteroaryl, heteroaralkyl; R5, R11 = H, alkyl, alkenyl, alkynyl, aryl cycloalkly, heterocyclylalkly, aralkyl, alkoxy, aryloxy, acyloxy, halo, OH, NH2, alkylseleno, arylseleno, etc.; R12 = H, alkly, alkenyl, alkynyl, aryl, cyclolalkyl, heterocyclylalkyl, OH, aralkyl, heteroaryl, haloalkyl, etc.; R15, R16, R17 = H, alkoxy, aryloxy, acyloxy, halo, OH, NH2, alkylamino, arylamino, etc.; R18, R19 = H, alkyl,aralkly, halo, amido, ester] or a pharmaceutically acceptable salt thereof, of cyclopamine that can be used to counteract the phenotypic effects of unwanted activation of a hedgehog pathway, such as resulting from hedgehog gain-of-function, Ptc loss-of-function or smoothened gain-of-function mutations. The present invention also provides analogs I {CR1R2, CR8R9 = C:O, C:S, C:NOR20, C:NR20 C:N-N(R20)2, (un)substituted 3- to 8-membered ring containing up to two heteroatoms selected from N, O, S; R4R5, R5R6, R10R11 = NR21, O, C(R23)2; R20 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaryl, heteroaralkyl; (R20)2 = (un)substituted 4- to 8-membered ring; R21 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaryl, heteroaralkyl, [C(R20)2]p-R25; (R21)2 = (un)substituted 4- to 8-membered ring with up to 3 heteroatoms selected from N, O, S, P; R23 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaryl, heteroaralkyl, halo, alkoxy, aryloxy, acyloxy, silyloxy, CN, C(:O)R21, CO2R21, SO2R21, C(:O)N(R21)2; R25 = H, OH, acylamino, N(R20)COR20, NR20C(:O)OR20, NR20SO2R20, C(OR20)N(R20)2, OC(:O)R20N(R20)2, SO2N(R20)2, N(R20)2, CO2R20, C(:O)N(OH)R21, OSO2OR20, SO3R20, OP(L)(OR20)2, NP(:O)(OR20)2, P(:O)(OR20)2; L = :O , :S; p = 0 - 6}. Thus, cyclopropane analog II (R = CH2CH2NHCO(CH2)5NHCOCH2CH2Ph; z = CH2) was preparation from cyclopamine (II; R = H, z = bond) via N-protection with Fmoc-succinimide in CH2Cl2, cyclopropanation with CH2I2 in CH2Cl2 containing Et2Zn in PhMe, deprotection with Et2NH in CH2Cl2 and reductive amination Ph(CH2)2CONH(CH2)5CONHCH2CHO with in MeCN containing NaBH(OAc)3. The compds. of the present invention are particularly useful in treating cancers. Inhibitory activity of II (R = CH2CH2NHCO(CH2)5NHCOCH2CH2Ph; z = CH2) upon cell differentiation was determined [EC50 = <200 nM].
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:220113 HCAPLUS
DOCUMENT NUMBER: 142:291381
TITLE: Hedgehog protein as angiogenesis-modulator and therapeutic uses thereof

```
INVENTOR(S):              Ling, Leona E.; Sanicola-Nadel, Michele; Kotkow,
                          Karen; Rubin, Lee L.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 113 pp., Cont.-in-part of U.S.
                          Ser. No. 883,848.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   7
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     US 20050054568       A1    20050310    US 2003-652686         20030829
     US 7498304           B2    20090303
     US 6552016           B1    20030422    US 2000-688018         20001013
     US 20030022819       A1    20030130    US 2001-883848         20010618
     US 20040023949       A1    20040205    US 2003-407551         20030404
     US 7300929           B2    20071127
PRIORITY APPLN. INFO.:                      US 2000-211919P     P  20000616
                                            US 2001-883848      A2 20010618
                                            US 2002-407445P     P  20020829
                                            US 1999-159417P     P  19991014
                                            US 2000-196543P     P  20000411
                                            US 2000-240536P     P  20001013
                                            US 2000-688018      A3 20001013
OTHER SOURCE(S):          MARPAT 142:291381
AB   The present invention relates to the use of hedgehog protein, DNA, or
     other hedgehog therapeutic as an agent to induce the growth of new blood
     vessels, angiogenesis, arteriogenesis or vascular growth in adult tissues
     where the induction of angiogenesis has therapeutic value.  The present
     invention also relates to the use of inhibitors of hedgehog protein or
     signaling to prevent angiogenesis contributing to pathol. conditions such
     as neoplasia (tumors and gliomas), diabetic retinopathy, rheumatoid
     arthritis, osteoarthritis, macular degeneration, psoriasis,
     ulcerative colitis, Crohn's disease, and inflammation.  Hedgehog agonists
     and antagonists can be used to regulate angiogenesis, and have utility in
     treating tissue repair and cancer, and to prevent angiogenesis driven
     pathologies.
REFERENCE COUNT:          169    THERE ARE 169 CITED REFERENCES AVAILABLE FOR
                                 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                                 FORMAT

L3   ANSWER 5 OF 7  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2004:674297  HCAPLUS
DOCUMENT NUMBER:          142:169369
TITLE:                    Rapid clearance of psoriatic skin lesions induced by
                          topical cyclopamine
AUTHOR(S):                Tas, Sinan; Avci, Oktay
CORPORATE SOURCE:         Samur Sokak 29/12, Ankara, Turk.
SOURCE:                   Dermatology (Basel, Switzerland) (2004), 209(2),
                          126-131
                          CODEN: DERAEG; ISSN: 1018-8665
PUBLISHER:                S. Karger AG
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   We have earlier found a highly efficient induction of the differentiation
     of epidermal lineage skin tumors by cyclopamine, a steroidal alkaloid
     inhibitor of the hedgehog/smoothened signaling, under conditions in which
     cyclopamine exerted no adverse effect on skin.  We aimed to develop a
     mechanism-based treatment for psoriasis with cyclopamine.  We
     subjected psoriatic skin lesions to cyclopamine under conditions similar
     to those we used for skin tumors and evaluated the responses of lesions
     clin. and by histopathol./immunohistochem. analyses.  All treated lesions
     in different patients having plaque and guttate forms of psoriasis
     regressed rapidly.  Differentiation of the epidermal cells of lesional
     skin and disappearances of infiltrating inflammatory cells were evident
     within a day.  Lesions were cleared commonly on days 3-4.  Former
     treatment sites followed up for more than 24 mo now show a lack of adverse
     effects in the long term.  An effective treatment for psoriasis
     is described, consistent with intervention in a proximal/key pathogenic
     event.
REFERENCE COUNT:         13    THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3   ANSWER 6 OF 7  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2004:312336  HCAPLUS
DOCUMENT NUMBER:         140:315109
TITLE:                   Use of cyclopamine in the treatment of
                         psoriasis
INVENTOR(S):             Tas, Sinan; Avci, Oktay
PATENT ASSIGNEE(S):      Turk.
SOURCE:                  U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of WO
                         2002 78,704.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  4
PATENT INFORMATION:

     PATENT NO.          KIND   DATE         APPLICATION NO.        DATE
     ---------------     ----   --------     --------------------   --------
     US 20040072913       A1    20040415     US 2003-682662         20031009
     WO 2002078703        A1    20021010     WO 2001-TR27           20010702
         W:  AT, AU, BR, CA, CN, DE, DK, ES, FI, GB, IN, JP, MX, NO, PT, RU,
             SE, TR, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     EP 1561464           A2    20050810     EP 2005-8758           20010702
     EP 1561464           A3    20070425
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY, TR
     WO 2002078704        A1    20021010     WO 2002-TR17           20020419
         W:  AT, AU, BR, CA, CN, DE, DK, ES, FI, GB, IN, JP, MX, NO, PT, RU,
             SE, TR, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     AU 2002309470        A1    20021015     AU 2002-309470         20020419
     CA 2481499           A1    20031030     CA 2003-2481499        20030317
     CA 2636960           A1    20031030     CA 2003-2636960        20030317
     WO 2003088964        A1    20031030     WO 2003-TR17           20030317
         W:  AT, AU, AZ, BR, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, ID, IN,
             JP, KR, MX, NO, NZ, PH, PL, PT, RO, RU, SE, TR, UA, US, ZA
         RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
             DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
             SI, SK, TR
     AU 2003230541        A1    20031103     AU 2003-230541         20030317
     AU 2003230541        B2    20060629
     EP 1496895           A1    20050119     EP 2003-723620         20030317
     EP 1496895           B1    20051116
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK
     BR 2003009396        A     20050209     BR 2003-9396           20030317
     AT 309802            T     20051215     AT 2003-723620         20030317
     JP 2006512281        T     20060413    JP 2003-585716          20030317
     ES 2253672           T3    20060601    ES 2003-723620          20030317
     CN 1835748           A     20060920    CN 2003-808784          20030317
     IN 2004DN00181       A     20050401    IN 2004-DN181           20040127
     IN 2004DN02987       A     20080808    IN 2004-DN2987          20040930
     MX 2004010294        A     20050517    MX 2004-10294           20041019
     IN 2007DN01029       A     20070803    IN 2007-DN1029          20070207
     US 20080090790       A1    20080417    US 2007-874653          20071018
     KR 2007108287        A     20071108    KR 2007-725034          20071030
     KR 2008094739        A     20081023    KR 2008-724137          20081001
     KR 2008096605        A     20081030    KR 2008-724138          20081001
PRIORITY APPLN. INFO.:                      WO 2001-TR27         A2 20010702
                                            WO 2002-TR17         A2 20020419
                                            EP 2001-952097       A3 20010702
                                            CA 2003-2481499      A3 20030317
                                            WO 2003-TR17         W  20030317
                                            US 2003-682662       A3 20031009
                                            IN 2004-DN2987       A3 20040930
                                            KR 2004-716679       A3 20041018
                                            KR 2007-725034       A3 20071030
AB   The invention discloses the use of cyclopamine, a naturally occurring
     steroidal alkaloid known for over thirty years, for the treatment of
     psoriasis and achievement of rapid clearance of the psoriatic skin
     lesions together with the reversion of the histopathol. signs of disease
     to normalcy with no detectable side effects.  The cyclopamine-induced
     clearance of psoriatic lesions from the skin of patients is associated with
     the causation of cellular differentiation in lesional epidermis and with
     the rapid disappearance of CD4+ lymphocytes and other inflammatory cells
     from lesional skin.  Therapeutic compns. comprising of cyclopamine and a
     corticosteroid and/or the pre-treatment of lesions with a corticosteroid
     provide significantly further increased therapeutic effectiveness over the
     use of cyclopamine alone or a corticosteroid alone.

L3   ANSWER 7 OF 7  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2002:793447  HCAPLUS
DOCUMENT NUMBER:          137:304813
TITLE:                    Modulators of hedgehog signaling pathway for treatment
                          of T-cell-mediated diseases
INVENTOR(S):              Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman,
                          Margaret Jane; Champion, Brian Robert
PATENT ASSIGNEE(S):       Lorantis Limited, UK
SOURCE:                   PCT Int. Appl., 154 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
     WO 2002080952        A2    20021017    WO 2002-GB1666          20020409
     WO 2002080952        A3    20040108
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2002247847          A1     20021021    AU 2002-247847          20020409
     EP 1401469             A2     20040331    EP 2002-716928          20020409
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004534743          T      20041118    JP 2002-578991          20020409
     US 20040126359         A1     20040701    US 2003-682230          20031009
PRIORITY APPLN. INFO.:                         GB 2001-8872         A  20010409
                                               GB 2001-8873         A  20010409
                                               WO 2002-GB1666       W  20020409
AB   Use of a modulator of a Hedgehog signaling pathway, or a modulator of a
     pathway which is a target of the Hedgehog signaling pathway in the preparation
     of a medicament for treatment of a disease or disorder associated with a
     T-cell mediated disease or disorder.
REFERENCE COUNT:         2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 15:39:41 ON 11 JUN 2009)

     FILE 'REGISTRY' ENTERED AT 15:39:53 ON 11 JUN 2009
L1             1 S CYCLOPAMINE/CN

     FILE 'HCAPLUS' ENTERED AT 15:40:11 ON 11 JUN 2009
L2           198 S L1
L3             7 S L2 AND PSORIASIS

=> s l1<chem>

   SmartSELECT INITIATED
New TRANSFER and ANALYZE Commands Now Available
See HELP TRANSFER and HELP ANALYZE for Details


COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    26.70      32.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -5.74      -5.74

FILE 'REGISTRY' ENTERED AT 15:41:27 ON 11 JUN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 American Chemical Society (ACS)

SET SMARTSELECT ON
SET COMMAND COMPLETED

SEL L1 1- CHEM
L4           SEL L1 1- CHEM :       6 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED


COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    15.08      47.83
```

```
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -5.74

FILE 'HCAPLUS' ENTERED AT 15:41:28 ON 11 JUN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

S L4
L5         413 L4

=> s l5 and psoriasis
         19153 PSORIASIS
L6           9 L5 AND PSORIASIS

=> d l6 1-9 ibib abs

L6   ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2009:170241  HCAPLUS
DOCUMENT NUMBER:         150:420035
TITLE:                   Lack of Evidence for Activation of the Hedgehog
                         Pathway in Psoriasis
AUTHOR(S):               Gudjonsson, Johann E.; Aphale, Abhishek; Grachtchouk,
                         Marina; Ding, Jun; Nair, Rajan P.; Wang, Timothy;
                         Voorhees, John J.; Dlugosz, Andrzej A.; Elder, James
                         T.
CORPORATE SOURCE:        Department of Dermatology, University of Michigan
                         Medical Center, Ann Arbor, MI, USA
SOURCE:                  Journal of Investigative Dermatology (2009), 129(3),
                         635-640
                         CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER:               Nature Publishing Group
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Recent reports have suggested that the hedgehog (Hh) pathway is activated
     in lesional psoriatic skin, and that treatment with the Hh pathway
     antagonist cyclopamine may lead to rapid resolution of the disease.
     To assess Hh pathway activity in psoriasis, we isolated RNA from
     lesional and uninvolved skin of 58 psoriatic patients, and from 63 normal
     control subjects, and subjected these samples to global gene expression
     profiling on Affymetrix HU133 Plus 2.0 gene arrays.  We were especially
     interested in Hh target genes (PTCH1 and GLI1), whose expression is
     elevated in response to Hh signaling.  The microarray data demonstrated
     downregulation of PTCH1 expression in uninvolved and lesional skin
     (1.1-fold and 2-fold, resp.; P<0.0001).  Addnl. GLI1 mRNA was
     downregulated in lesional skin (1.7 fold; P<0.05).  No significant changes
     were observed between lesional and uninvolved skin for the Hh ligands or
     Smoothened.  Quant. PCR confirmed these findings.  In situ hybridization
     for GLI1 and PTCH1 was pos. in basal cell carcinoma tumor cells, but was
     negligible in uninvolved or lesional psoriatic skin.  The absence of
     elevated Hh target gene expression in lesional psoriatic skin indicates
     that the Hh pathway is not activated in this disease, raising questions
     regarding the proposed use of Hh antagonists as antipsoriatic agents.
REFERENCE COUNT:         38    THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 2 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2007:1392120  HCAPLUS
DOCUMENT NUMBER:         148:24502
TITLE:                   Hexahydropyrimidine derivatives, tetrahydroimidazole
                         derivatives, and octahydroazepan derivatives, and
                         their therapeutic use
INVENTOR(S):             Westman, Jacob; Toftgaard, Rune; Lauth, Mattias;
                         Teglund, Stephan
PATENT ASSIGNEE(S):      Actar AB, Swed.
SOURCE:                  PCT Int. Appl., 55pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2007139492        A1    20071206    WO 2007-SE50352        20070524
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,
             GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
             KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK,
             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                      SE 2006-1188        A  20060530
OTHER SOURCE(S):         MARPAT 148:24502
GI
```



I

```
AB   The invention discloses compds. I [R1 = (un)substituted (un)branched
     (un)saturated C3-12 cycloalkyl and C1-10 alkyl, etc.; R2-R5 = H, halo, OH,
     etc.; n = 0-2] for use as medicaments.  The medicaments are suitable for
     the treatment of conditions such as cancer, keloids and granulomatous skin
     disorders, psoriasis, pathol. neovascularization, excessive hair
     growth and excessive body weight and for inhibition of stem cell
     proliferation and induction of differentiation after spinal cord injury
     and CNS diseases.  The invention also discloses a method for treating a
     mammal by administration of I.
REFERENCE COUNT:         11    THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 3 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2007:227086  HCAPLUS
DOCUMENT NUMBER:         146:280997
TITLE:                   Hedgehog pathway antagonists to treat disease
```

```
INVENTOR(S):              Beachy, Philip Arden; Liu, Jun
PATENT ASSIGNEE(S):       The Johns Hopkins University, USA
SOURCE:                   PCT Int. Appl., 46pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2007024971        A2    20070301    WO 2006-US32952        20060822
     WO 2007024971        A3    20080103
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
     AU 2006283040        A1    20070301    AU 2006-283040         20060822
     CA 2619889           A1    20070301    CA 2006-2619889        20060822
     EP 1919480           A2    20080514    EP 2006-802186         20060822
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
             BA, HR, MK, RS
     JP 2009506054        T     20090212    JP 2008-528124         20060822
PRIORITY APPLN. INFO.:                      US 2005-710117P     P  20050822
                                            WO 2006-US32952     W  20060822
AB   Compds., compns., kits and methods for modulating hedgehog pathway
     activity, and treating conditions such as tumors related to abnormal or
     aberrant hedgehog pathway activity, are disclosed wherein the hedgehog
     antagonist is itraconazole.

L6   ANSWER 4 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2006:464185  HCAPLUS
DOCUMENT NUMBER:          145:353375
TITLE:                    Psoriatic skin expresses the transcription factor
                          Gli1: possible contribution of decreased neurofibromin
                          expression
AUTHOR(S):                Endo, H.; Momota, Y.; Oikawa, A.; Shinkai, H.
CORPORATE SOURCE:         Department of Dermatology, Chiba Aoba Municipal
                          Hospital, 1273-2 Aoba-cho, Chuo-ku, Chiba, 260-0852,
                          Japan
SOURCE:                   British Journal of Dermatology (2006), 154(4), 619-623
                          CODEN: BJDEAZ; ISSN: 0007-0963
PUBLISHER:                Blackwell Publishing Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Background: Psoriasis is a chronic inflammatory disorder of skin
     characterized by hyperproliferation of keratinocytes.  Intracellular
     signalling pathways inducing the hyperproliferation of keratinocytes
     remain to be elucidated.  An inhibitor of Hedgehog (Hh) signaling,
     cyclopamine, was recently reported to clear psoriatic skin
     lesions, suggesting involvement of the Hh signalling pathway in the
     hyperproliferation of lesional keratinocytes.  We have previously observed
     activation of the Hh signaling pathway in Schwann cells of plexiform
     neurofibroma in neurofibromatosis type 1 (NF1), which results from
     functional loss of the NF1 encoding protein, neurofibromin.  In
     psoriasis, deficiency of neurofibromin expression has been observed
     in lesional keratinocytes.  Objectives: To investigate whether the Hh
     signalling pathway would be activated in psoriasis and whether
     inhibition of neurofibromin expression would enhance the activation of the
     Hh signaling pathway.  Methods: Activation of the Hh signaling pathway was
     examined by protein expression of one of the target genes, GLI1, coding for
     the transcription factor Gli1.  Immunohistochem. studies were performed on
     seven psoriatic skin samples and seven control normal skin samples with a
     standard immunoperoxidase technique.  MRNA expression of GLI1 was analyzed by
     reverse transcriptase-polymerase chain reaction in HaCaT cells transfected
     with double-strand small interfering RNA for NF1.  Results: Our results
     showed Gli1 expression in psoriatic skin but not in control normal skin.
     Inhibition of neurofibromin expression in HaCaT cells upregulated mRNA
     expression of GLI1.  Conclusions: Our findings indicate that the Hh
     signaling pathway is activated in psoriasis and that
     neurofibromin deficiency may upregulate the pathway.
REFERENCE COUNT:         23    THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 5 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2006:213263  HCAPLUS
DOCUMENT NUMBER:         144:292926
TITLE:                   Methods for preparation cyclopamine analogs
                         and use thereof in treating cancers
INVENTOR(S):             Janardanannair, Somarajannair; Adams, Julian; Ripka,
                         Amy S.; Hospital, Marta R.; Tremblay, Martin
PATENT ASSIGNEE(S):      Infinity Pharmaceuticals, Inc., USA
SOURCE:                  PCT Int. Appl., 102 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
     ---------------     ----   --------   --------------------   --------
     WO 2006026430        A2    20060309   WO 2005-US30406        20050826
     WO 2006026430        A3    20060622
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     AU 2005280112        A1    20060309   AU 2005-280112         20050826
     CA 2579078           A1    20060309   CA 2005-2579078        20050826
     US 20060074030       A1    20060406   US 2005-213534         20050826
     US 7230004           B2    20070612
     EP 1817308           A2    20070815   EP 2005-791140         20050826
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
             BA, HR, MK, YU
     CN 101044139         A     20070926   CN 2005-80035365       20050826
     JP 2008511635        T     20080417   JP 2007-530162         20050826
```

BR 2005014444	A	20080610	BR 2005-14444		20050826
MX 2007002342	A	20080627	MX 2007-2342		20070226
IN 2007KN00744	A	20070713	IN 2007-KN744		20070228
NO 2007001264	A	20070515	NO 2007-1264		20070308
KR 2007083602	A	20070824	KR 2007-706979		20070327
US 20070191410	A1	20070816	US 2007-737035		20070418
US 7407967	B2	20080805			
US 20080269272	A1	20081030	US 2008-171208		20080710
PRIORITY APPLN. INFO.:			US 2004-605020P	P	20040827
			US 2004-617170P	P	20041008
			US 2004-625676P	P	20041105
			US 2005-683169P	P	20050519
			US 2005-213534	A1	20050826
			WO 2005-US30406	W	20050826
			US 2007-737035	A1	20070418

OTHER SOURCE(S): CASREACT 144:292926; MARPAT 144:292926

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides compns. and methods for modulating smoothened dependent pathway activation. The present invention provides analogs I [R1, R8 = H, alkyl, alkenyl, alkynyl, aryl cycloalkly, heterocyclylalkly, aralkyl, heteroaryl, heteroaralkyl, halo, SH, alkylthio, arylthio, aralkylthio, OH, alkoxy, aryloxy, acyloxy, NH2, mono- or dialkylamino, arylamino, acylamino, aralkylamino, NO2, acylthio, CONH2, SO2NH2, sulfate, etc.; R1 = sugar; R2, R9 = H, alkyl, alkenyl, alkynyl, aryl cycloalkyl, heterocyclylalkyl, CN, aralkyl, alkoxy, aryloxy, acyloxy, CO2H, halo, SH, alkylhio, arylthio, aralkylthio, OH, NH2, alkylamino, arylamino, acylamino, aralkylamino, etc.; R3, R4, R6, R7, R13, R14 = H, alkyl, alkenyl, alkynyl, aryl cycloalkyl, heterocyclylalkyl, aralkyl, alkoxy, aryloxy, acyloxy, halo, OH, NH2, alkylamino, arylamino, acylamino, aralkylamino, heteroaryl, heteroaralkyl; R5, R11 = H, alkyl, alkenyl, alkynyl, aryl cycloalkly, heterocyclylalkly, aralkyl, alkoxy, aryloxy, acyloxy, halo, OH, NH2, alkylseleno, arylseleno, etc.; R12 = H, alkly, alkenyl, alkynyl, aryl, cyclolalkyl, heterocyclylalkyl, OH, aralkyl, heteroaryl, haloalkyl, etc.; R15, R16, R17 = H, alkoxy, aryloxy, acyloxy, halo, OH, NH2, alkylamino, arylamino, etc.; R18, R19 = H, alkyl,aralkly, halo, amido, ester] or a pharmaceutically acceptable salt thereof, of cyclopamine that can be used to counteract the phenotypic effects of unwanted activation of a hedgehog pathway, such as resulting from hedgehog gain-of-function, Ptc loss-of-function or smoothened gain-of-function mutations. The present invention also provides analogs I {CR1R2, CR8R9 = C:O, C:S, C:NOR20, C:NR20 C:N-N(R20)2, (un)substituted 3- to 8-membered ring containing up to two heteroatoms selected from N, O, S; R4R5, R5R6, R10R11 = NR21, O, C(R23)2; R20 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaryl, heteroaralkyl; (R20)2 = (un)substituted 4- to 8-membered ring; R21 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaryl, heteroaralkyl, [C(R20)2]p-R25; (R21)2 = (un)substituted 4- to 8-membered ring with up to 3 heteroatoms selected from N, O, S, P; R23 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaryl, heteroaralkyl, halo, alkoxy, aryloxy, acyloxy, silyloxy, CN, C(:O)R21, CO2R21, SO2R21, C(:O)N(R21)2; R25 = H, OH, acylamino, N(R20)COR20, NR20C(:O)OR20, NR20SO2R20, C(OR20)N(R20)2, OC(:O)R20N(R20)2, SO2N(R20)2, N(R20)2, CO2R20, C(:O)N(OH)R21, OSO2OR20, SO3R20, OP(L)(OR20)2, NP(:O)(OR20)2, P(:O)(OR20)2; L = :O , :S; p = 0 - 6}. Thus, cyclopropane analog II (R = CH2CH2NHCO(CH2)5NHCOCH2CH2Ph; z = CH2) was preparation from cyclopamine (II; R = H, z = bond) via N-protection with

```
     Fmoc-succinimide in CH2Cl2, cyclopropanation with CH2I2 in CH2Cl2 containing
     Et2Zn in PhMe, deprotection with Et2NH in CH2Cl2 and reductive amination
     Ph(CH2)2CONH(CH2)5CONHCH2CHO with in MeCN containing NaBH(OAc)3.  The compds.
     of the present invention are particularly useful in treating cancers.
     Inhibitory activity of II (R = CH2CH2NHCO(CH2)5NHCOCH2CH2Ph; z = CH2) upon
     cell differentiation was determined [EC50 = <200 nM].
REFERENCE COUNT:         1     THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 6 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2005:220113  HCAPLUS
DOCUMENT NUMBER:         142:291381
TITLE:                   Hedgehog protein as angiogenesis-modulator and
                         therapeutic uses thereof
INVENTOR(S):             Ling, Leona E.; Sanicola-Nadel, Michele; Kotkow,
                         Karen; Rubin, Lee L.
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 113 pp., Cont.-in-part of U.S.
                         Ser. No. 883,848.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  7
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
     ---------------     ----   --------   --------------------   --------
     US 20050054568       A1    20050310   US 2003-652686         20030829
     US 7498304           B2    20090303
     US 6552016           B1    20030422   US 2000-688018         20001013
     US 20030022819       A1    20030130   US 2001-883848         20010618
     US 20040023949       A1    20040205   US 2003-407551         20030404
     US 7300929           B2    20071127
PRIORITY APPLN. INFO.:                     US 2000-211919P     P  20000616
                                           US 2001-883848      A2 20010618
                                           US 2002-407445P     P  20020829
                                           US 1999-159417P     P  19991014
                                           US 2000-196543P     P  20000411
                                           US 2000-240536P     P  20001013
                                           US 2000-688018      A3 20001013
OTHER SOURCE(S):         MARPAT 142:291381
AB   The present invention relates to the use of hedgehog protein, DNA, or
     other hedgehog therapeutic as an agent to induce the growth of new blood
     vessels, angiogenesis, arteriogenesis or vascular growth in adult tissues
     where the induction of angiogenesis has therapeutic value.  The present
     invention also relates to the use of inhibitors of hedgehog protein or
     signaling to prevent angiogenesis contributing to pathol. conditions such
     as neoplasia (tumors and gliomas), diabetic retinopathy, rheumatoid
     arthritis, osteoarthritis, macular degeneration, psoriasis,
     ulcerative colitis, Crohn's disease, and inflammation.  Hedgehog agonists
     and antagonists can be used to regulate angiogenesis, and have utility in
     treating tissue repair and cancer, and to prevent angiogenesis driven
     pathologies.
REFERENCE COUNT:         169   THERE ARE 169 CITED REFERENCES AVAILABLE FOR
                               THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                               FORMAT

L6   ANSWER 7 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2004:674297  HCAPLUS
DOCUMENT NUMBER:         142:169369
TITLE:                   Rapid clearance of psoriatic skin lesions induced by
                         topical cyclopamine
```

```
AUTHOR(S):               Tas, Sinan; Avci, Oktay
CORPORATE SOURCE:        Samur Sokak 29/12, Ankara, Turk.
SOURCE:                  Dermatology (Basel, Switzerland) (2004), 209(2),
                         126-131
                         CODEN: DERAEG; ISSN: 1018-8665
PUBLISHER:               S. Karger AG
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   We have earlier found a highly efficient induction of the differentiation
     of epidermal lineage skin tumors by cyclopamine, a steroidal
     alkaloid inhibitor of the hedgehog/smoothened signaling, under conditions
     in which cyclopamine exerted no adverse effect on skin.  We
     aimed to develop a mechanism-based treatment for psoriasis with
     cyclopamine.  We subjected psoriatic skin lesions to
     cyclopamine under conditions similar to those we used for skin
     tumors and evaluated the responses of lesions clin. and by
     histopathol./immunohistochem. analyses.  All treated lesions in different
     patients having plaque and guttate forms of psoriasis regressed
     rapidly.  Differentiation of the epidermal cells of lesional skin and
     disappearances of infiltrating inflammatory cells were evident within a
     day.  Lesions were cleared commonly on days 3-4.  Former treatment sites
     followed up for more than 24 mo now show a lack of adverse effects in the
     long term.  An effective treatment for psoriasis is described,
     consistent with intervention in a proximal/key pathogenic event.
REFERENCE COUNT:         13    THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 8 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2004:312336  HCAPLUS
DOCUMENT NUMBER:         140:315109
TITLE:                   Use of cyclopamine in the treatment of
                         psoriasis
INVENTOR(S):             Tas, Sinan; Avci, Oktay
PATENT ASSIGNEE(S):      Turk.
SOURCE:                  U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of WO
                         2002 78,704.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  4
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
     ---------------     ----   --------   --------------------   --------
     US 20040072913       A1    20040415   US 2003-682662         20031009
     WO 2002078703        A1    20021010   WO 2001-TR27           20010702
         W:  AT, AU, BR, CA, CN, DE, DK, ES, FI, GB, IN, JP, MX, NO, PT, RU,
             SE, TR, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     EP 1561464           A2    20050810   EP 2005-8758           20010702
     EP 1561464           A3    20070425
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY, TR
     WO 2002078704        A1    20021010   WO 2002-TR17           20020419
         W:  AT, AU, BR, CA, CN, DE, DK, ES, FI, GB, IN, JP, MX, NO, PT, RU,
             SE, TR, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     AU 2002309470        A1    20021015   AU 2002-309470         20020419
     CA 2481499           A1    20031030   CA 2003-2481499        20030317
     CA 2636960           A1    20031030   CA 2003-2636960        20030317
     WO 2003088964        A1    20031030    WO 2003-TR17           20030317
         W:  AT, AU, AZ, BR, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, ID, IN,
             JP, KR, MX, NO, NZ, PH, PL, PT, RO, RU, SE, TR, UA, US, ZA
         RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
             DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
             SI, SK, TR
     AU 2003230541        A1    20031103    AU 2003-230541         20030317
     AU 2003230541        B2    20060629
     EP 1496895           A1    20050119    EP 2003-723620         20030317
     EP 1496895           B1    20051116
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK
     BR 2003009396        A     20050209    BR 2003-9396           20030317
     AT 309802            T     20051215    AT 2003-723620         20030317
     JP 2006512281        T     20060413    JP 2003-585716         20030317
     ES 2253672           T3    20060601    ES 2003-723620         20030317
     CN 1835748           A     20060920    CN 2003-808784         20030317
     IN 2004DN00181       A     20050401    IN 2004-DN181          20040127
     IN 2004DN02987       A     20080808    IN 2004-DN2987         20040930
     MX 2004010294        A     20050517    MX 2004-10294          20041019
     IN 2007DN01029       A     20070803    IN 2007-DN1029         20070207
     US 20080090790       A1    20080417    US 2007-874653         20071018
     KR 2007108287        A     20071108    KR 2007-725034         20071030
     KR 2008094739        A     20081023    KR 2008-724137         20081001
     KR 2008096605        A     20081030    KR 2008-724138         20081001
PRIORITY APPLN. INFO.:                      WO 2001-TR27        A2 20010702
                                            WO 2002-TR17        A2 20020419
                                            EP 2001-952097      A3 20010702
                                            CA 2003-2481499     A3 20030317
                                            WO 2003-TR17        W  20030317
                                            US 2003-682662      A3 20031009
                                            IN 2004-DN2987      A3 20040930
                                            KR 2004-716679      A3 20041018
                                            KR 2007-725034      A3 20071030
```

AB The invention discloses the use of cyclopamine, a naturally occurring steroidal alkaloid known for over thirty years, for the treatment of psoriasis and achievement of rapid clearance of the psoriatic skin lesions together with the reversion of the histopathol. signs of disease to normalcy with no detectable side effects. The cyclopamine-induced clearance of psoriatic lesions from the skin of patients is associated with the causation of cellular differentiation in lesional epidermis and with the rapid disappearance of CD4+ lymphocytes and other inflammatory cells from lesional skin. Therapeutic compns. comprising of cyclopamine and a corticosteroid and/or the pre-treatment of lesions with a corticosteroid provide significantly further increased therapeutic effectiveness over the use of cyclopamine alone or a corticosteroid alone.

```
L6   ANSWER 9 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2002:793447  HCAPLUS
DOCUMENT NUMBER:         137:304813
TITLE:                   Modulators of hedgehog signaling pathway for treatment
                         of T-cell-mediated diseases
INVENTOR(S):             Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman,
                         Margaret Jane; Champion, Brian Robert
PATENT ASSIGNEE(S):      Lorantis Limited, UK
SOURCE:                  PCT Int. Appl., 154 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:
     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
     ---------------     ----   --------   --------------------   --------
     WO 2002080952        A2    20021017   WO 2002-GB1666         20020409
     WO 2002080952        A3    20040108
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2002247847        A1    20021021   AU 2002-247847         20020409
     EP 1401469           A2    20040331   EP 2002-716928         20020409
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004534743        T     20041118   JP 2002-578991         20020409
     US 20040126359       A1    20040701   US 2003-682230         20031009
PRIORITY APPLN. INFO.:                     GB 2001-8872        A  20010409
                                           GB 2001-8873        A  20010409
                                           WO 2002-GB1666      W  20020409
AB   Use of a modulator of a Hedgehog signaling pathway, or a modulator of a
     pathway which is a target of the Hedgehog signaling pathway in the preparation
     of a medicament for treatment of a disease or disorder associated with a
     T-cell mediated disease or disorder.
REFERENCE COUNT:         2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 15:39:41 ON 11 JUN 2009)

     FILE 'REGISTRY' ENTERED AT 15:39:53 ON 11 JUN 2009
L1            1 S CYCLOPAMINE/CN

     FILE 'HCAPLUS' ENTERED AT 15:40:11 ON 11 JUN 2009
L2          198 S L1
L3            7 S L2 AND PSORIASIS

     FILE 'REGISTRY' ENTERED AT 15:41:27 ON 11 JUN 2009
                SET SMARTSELECT ON
L4          SEL L1 1- CHEM :       6 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 15:41:28 ON 11 JUN 2009
L5          413 S L4
L6            9 S L5 AND PSORIASIS

=>

---Logging off of STN---



=>
Executing the logoff script...
```

```
=> LOG Y

COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    29.85      77.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -7.38     -13.12

STN INTERNATIONAL LOGOFF AT 15:42:05 ON 11 JUN 2009
```